

Can the Neutrophil-to-Platelet Ratio Be Used to Predict Postoperative Mortality in Geriatric Patients with Hip Fractures?

Tugcehan Sezer Akman¹, Hatice Kusderci², Lokman Kehribar³, Bahattin Cagdas Akman⁴, Ahmet Sen⁵

¹Anesthesiology and Reanimation, Alaca State Hospital, Alaca, Corum, Türkiye

²Department of Anesthesiology and Reanimation, University of Samsun, Samsun, Türkiye

³Department of Orthopedics and Traumatology, University of Samsun, Samsun, Türkiye

⁴Orthopedics and Traumatology, Alaca State Hospital, Alaca, Corum, Türkiye

⁵Department of Anesthesiology and Reanimation, Trabzon Kanuni Training and Research Hospital, Trabzon, Türkiye

Address for Correspondence: Anesthesiology and Reanimation, Alaca State Hospital, Yıldızhan Neighbourhood Cengiztopel Street, No: 124 Alaca- Corum- Türkiye
Email: tgchnszr@gmail.com

Orcid ID: TSA: 0000-0003-4135-840 LK: 0000-0001-9799-8839 AS: 0000-0001-8981-6871
HK: 000-0002-3963-3265 BCA: 0000-0002-1439-9863

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Abstract

Objective: Hip fracture is a condition frequently encountered in geriatric patients and is correlated with high postoperative mortality and morbidity. Numerous factors may impact mortality, but recent studies have focused on its correlation with inflammation. The neutrophil-to-platelet ratio has been evaluated as a systemic inflammation marker. The aim of our study was to examine the correlation between preoperative neutrophil-to-platelet ratio (NPR) values and postoperative one-year mortality in geriatric patients with hip fractures.

Material and Method: In our retrospective, multicenter study, 50 patients over 65 years of age who had undergone hip fracture surgery under spinal anesthesia were examined. Patients' preoperative neutrophil-to-platelet ratio values at the time of hospitalization, age, gender, American Society of Anesthesiologists scores, fracture types, comorbidities, durations of surgery, lengths of hospital stay, and survival in the postoperative one-year period were checked.

Results: The mean age of all the patients was 85.44 ± 6.93 years. Of the patients, 60% were female ($n = 30$), and 40% were male ($n = 20$). The optimal cut-off value for preoperative neutrophil-to-platelet ratio was specified as 38.286. The length of hospital stay was 8.94 ± 3.05 in the deceased patients and 6.94 ± 2.63 days ($p = 0.02$) in the surviving group. The mortality rate was higher in men than in women ($p = 0.01$).

Conclusion: A preoperative neutrophil-to-platelet ratio value over 38.286 is an indicator of postoperative one-year mortality in elderly hip fracture patients. Additionally, length of hospital stay and the male gender were revealed to be correlated with mortality.

Keywords: Geriatrics, Hip Fractures, Mortality, Inflammation

Özet

Amaç: Kalça kırığı, geriyatrik hastalarda sıklıkla karşılaşılan bir durumdur ve yüksek postoperatif mortalite ve morbidite ile ilişkilidir. Mortaliteyi etkileyebilecek çok sayıda faktör vardır, ancak son çalışmalar inflamasyon ile ilişkisine odaklanmıştır. Nötrofil-platelet oranı, sistemik bir inflamasyon belirteci olarak kullanılmaktadır. Çalışmamızın amacı, kalça kırığı olan geriyatrik hastalarda ameliyat öncesi nötrofil-platelet oranı (NPR) değerleri ile ameliyat sonrası bir yıllık mortalite arasındaki ilişkiyi incelemektir.

Gereç ve Yöntem: Retrospektif, çok merkezli çalışmamızda spinal anestezi altında kalça kırığı ameliyatı geçirmiş 65 yaş üstü 50 hasta incelendi. Hastaların preoperatif hastaneye yatış anındaki nötrofil-platelet oranı değerleri, yaşları, cinsiyetleri, Amerikan Anesteziyologlar Derneği skorları (ASA), kırık tipleri, komorbiditeleri, cerrahi süreleri, hastanede kalış süreleri ve postoperatif bir yıllık dönemde sağkalımları incelendi.

Bulgular: Tüm hastaların ortalama yaşı $85,44 \pm 6,93$ idi. Hastaların %60'ı kadın ($n=30$), %40'ı erkekti ($n=20$). Ameliyat öncesi nötrofil-platelet oranı için optimal cut-off değeri 38.286 olarak belirlendi. Hastanede kalış süresi ölen hastalarda $8,94 \pm 3,05$, yaşayan grupta $6,94 \pm 2,63$ gün ($p=0,02$) bulundu. Erkeklerde ölüm oranı kadınlara göre daha yüksekti ($p=0,01$).

Sonuç: Ameliyat öncesi nötrofil-platelet oranı değerinin 38.286'nın üzerinde olması, yaşlı kalça kırığı hastalarında ameliyat sonrası bir yıllık mortalitenin göstergesi olarak bulundu. Ayrıca hastanede kalış süresi ve erkek cinsiyetin mortalite ile ilişkili olduğu kanıtlanmıştır.

Anahtar Sözcükler: Geriyatri, Kalça Kırığı, Mortalite, İnflamasyon

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Complaints: hmj@hitit.edu.tr

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Introduction

Hip fracture is a condition that is frequently seen in elderly patients and progresses with high postoperative mortality and other complications. The mortality rate is 1–7.2% in the first postoperative month, but reaches 8.4–36% in a year (1,2). The highest mortality rate after hip fractures is seen in the first six months, after which the rate decreases (3). Mortality is impacted by numerous factors, such as age, gender, functional status before fracture, type of surgery, comorbidities, length of hospital stay, preoperative hemoglobin level, a low body mass index, malnutrition, and a high American Society of Anesthesiologists (ASA) score (3-6).

Inflammation has been found to be correlated with the onset or progression of many diseases, such as cancers associated with high mortality and morbidity, atherosclerosis, and sickle cell anemia (7). In recent studies, it has been asserted that inflammatory markers may independently affect short- and long-term mortality after hip fractures (1). There are series of studies indicating the correlation between inflammation-based markers that reflect systemic inflammation, such as, C-reactive protein (CRP), ferritin, transferrin, interleukin 6 (IL-6), soluble urokinase plasminogen activator receptor (suPAR), the prognostic nutritional index (PNI), tumor necrosis factor-alpha (TNF-alpha), the systemic immune inflammation index (SII), the CRP/PNI ratio, and the neutrophil/lymphocyte ratio (NLR), and postoperative poor prognosis and complications in patients with hip fractures (1,4,8,9). The neutrophil to platelet ratio (NPR) has been specified as a marker of systemic inflammation and has been associated with conditions such as ulcerative colitis, infective endocarditis, thromboembolic events, acute appendicitis, and hemorrhagic transformation in acute ischemic stroke (10-13). However, no publications have been found in the literature regarding its correlation with mortality in geriatric patients with hip fractures.

The aim of our study was to examine the correlation between preoperative NPR values and postoperative one-year mortality in geriatric patients with hip fractures.

Material and Method

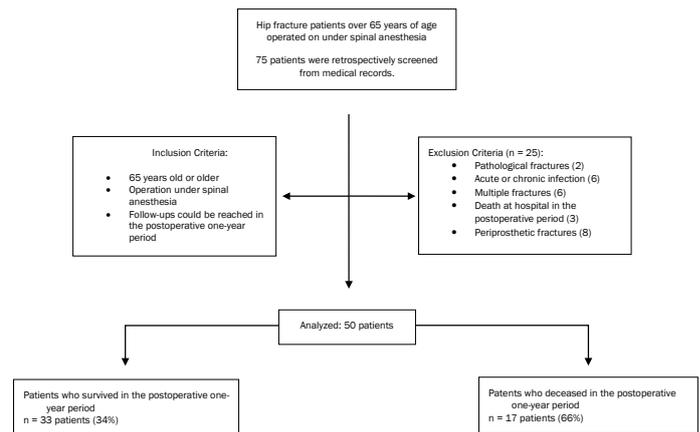
1. Ethical Considerations

Approval from Ethics Committee was obtained for this retrospective, observational study, which was carried out in accordance with the Declaration of Helsinki.

2. Patient Population and Data Collection

Seventy-five patients over 65 years of age who had been operated on for hip fracture under spinal anesthesia between January 2021 and January 2022 in the two centers were retrospectively screened, and their information and follow-ups in the postoperative one-year period were acquired via medical records (computer system) and telephone. Exclusion criteria were set as patients having pathological fractures, high-energy traumas, acute or chronic infections, multiple fractures, and death at the hospital in the postoperative period. Six patients had multiple fractures, six had acute infections, three died at hospital in the postoperative period, eight had periprosthetic fractures, and two had pathological fractures. Therefore, they were excluded from consideration, and the study was conducted on the remaining 50 patients (Figure I).

Figure I. Diagram of the Study Design



The patients' ages, genders, fracture types, ASA scores, lengths of hospital stay, comorbidities, preoperative NPR values, and survival-mortality statuses in a year were recorded. When patients were admitted to the hospital, venous blood samples studied in the preoperative period were used for NPR calculation. While calculating the NPR value, the formula of neutrophil count (109/L) x 1000/platelet count (109/L) was used.

Statistical Analysis

SPSS software version 20.0 (IBM Corp., Armonk, NY) was used to conduct the statistical analyses. Descriptive statistics were presented as means, medians, standard deviations, ranges, and percentages. The normality of the data was tested using the Shapiro–Wilk test. Pearson's chi-square test was performed to analyze the categorical variables appropriately. To analyze the continuous variables, the independent samples t-test was used wherever suitable. Receiver operating characteristic (ROC) analysis was used to identify the threshold value of NPR for mortality, and thus to divide patients into high or low NPR groups. To reveal the prognostic factors predicting one-year mortality following hip fracture surgery, bilateral logistic regression was carried out for the important variables in the univariate analysis through the forward stepwise conditional method. Probability rates were calculated with 95% confidence intervals (CIs). The value of $p < 0.05$ was considered statistically significant. The minimum sample size required to detect a significant difference using this test should be at least 15 in each group, (30 in total), considering type I error (alpha) of 0.05, power (1-beta) of 0.8, effect size of 1.07 and two-sided alternative hypothesis (H1). However, considering the risk of any problems with the patients, it was thought that it would be appropriate to work with a total of 50 people in the study.

Results

In this study, in which 50 patients were involved in the analysis, the mean age of all patients was 85.44 ± 6.93 years (min: 70, max: 96; Table I). Of all the patients, 60% were female ($n = 30$), and 40% were male ($n = 20$; Table II). Furthermore, 86% ($n = 43$) were in the high-risk group (ASA3–4), and 14% ($n = 7$) were in the low-risk group (ASA1–2; Table II). The most observed type of fracture was femoral neck fracture (44%), followed by pertrochanteric (24%), intertrochanteric (18%), basicervical (8%), and subtrochanteric (6%) fractures,

Table I. Correlation Between Age, Duration of Surgery, Length of Hospital Stay and Survival of Patients

Variable	Surviving group Mean±SD (range).	Deceased group Mean±SD (range).	Total Mean±SD (range).	p-value
Age (years)	84.94 ± 7.03 (70-96)	86.41 ± 5.17 (74-94)	85.44 ± 6.44 (70-96)	0.454
Duration of surgery (minutes)	94.61 ± 31.03 (49-160)	95.47 ± 30.53 (49-145)	94.9±30.56 (49-160)	0.926
Length of hospital stay (days)	6.94 ± 2.63 (3-12)	8.94 ± 3.05 (4-14)	7.63 ± 2.91 (3-14)	0.02*

Independent samples t-test was used. *p < 0.05 was considered significant.

Table II. Correlation Between Patients' Demographic Information and Survival

Variable	Surviving group n (%)	Deceased group n (%)	Total n (%)	p-value
	33 (66)	17 (34)	50	
Gender				
Female	24 (80)	6 (20)	30 (60)	0.01*
Male	9 (45)	11 (55)	20 (40)	
ASA				
1-2 (low risk)	5 (71.4)	2 (28.6)	7 (14)	0.744
3-4 (high risk)	28 (65.1)	15 (34.9)	43 (86)	
Comorbidity				
None	7 (77.8)	2 (22.2)	9 (18)	0.439
1--2	21 (67.7)	10 (32.3)	31 (62)	
3 and above	5 (50)	5 (50)	10 (20)	
Fracture type				
Basicervical	1 (25)	3 (75)	4 (8)	0.162
Femoral neck	17 (77.3)	5 (22.7)	22 (44)	
Intertrochanteric	4 (44.4)	5 (55.6)	9 (18)	
Pertrochanteric	9 (75)	3 (25)	12 (24)	
Subtrochanteric	2 (66.7)	1 (33.3)	3 (6)	

Pearson's chi-square test was used. *p < 0.05 was considered significant. n: Number

respectively (Table II). The mean operation time of all patients was 94.9 ± 30.56 min (min: 49 min, max: 160 min), and the mean length of hospital stay was 7.63 ± 2.91 days (min: three days, max: 14 days; Table I). The most frequent comorbidities were diabetes mellitus, hypertension, and coronary artery disease, respectively (Table III).

Of all patients, 34% (n = 17) had deceased in the one-year postoperative period. The patients were categorized as surviving or deceased according to their one-year postoperative survival (Table I, Table II). According to the ROC curve analysis, the optimal cut-off value for preoperative NPR was found to be 38.286 (sensitivity: 66.7%, specificity: 64.7%) (Figure 2). The NPR value was 58.07 ± 44.14 (min: 15.47, max: 202.83) in the deceased patient group and 33.34 ± 17.64 (min: 10.70, max: 76.83) in the surviving patient group.

The mean age of the surviving patients was 84.94 ± 7.03 years (min: 70, max: 96), while the mean age of the deceased patients was 86.41 ± 5.17 years (min: 74, max: 94). No statistical difference was observed (p = 0.454; Table I). When the two groups were categorized as low risk (ASA1-2) and high risk (ASA3-4) groups according to the ASA score, five people from the surviving group were assessed to be in the low-risk group, and 28 people were assigned to the high-risk group. From the deceased group, two people were evaluated in the low-risk group, and 15 people were

Figure II. ROC curve of NPR for predicting 1-year mortality. Data presented as area under the curve (AUC) with 95% confidence interval (CI)

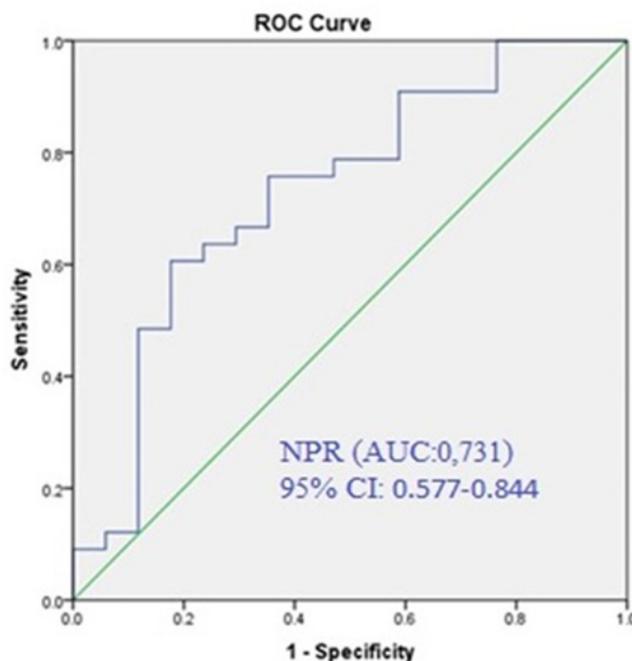


Table III. Accompanying Comorbid Diseases

Comorbid diseases	N (%)
Diabetes mellitus	15 (20.3)
Hypertension	16 (21.6)
Coronary artery diseases	10 (13.5)
Cerebrovascular disease	9 (12.2)
Chronic obstructive pulmonary disease	5 (6.8)
Chronic renal failure	5 (6.8)
Alzheimer's disease	5 (6.8)
Congestive heart failure	8 (10.8)
Parkinson's disease	1 (1.4)

assigned to the high-risk group. No statistical difference was determined between the two groups (p = 0.744).

The patients were classified into three groups based on whether their number of comorbidities was 1-2, three, or above, and there was no statistical difference between the surviving and deceased groups in this respect (p = 0.439; Table II). The mean length of hospital stay was 6.94 ± 2.63 days (min: 3, max: 12 days) in the surviving group and 8.94 ± 3.05 days (min: 4, max: 14 days) in the deceased group. The length of hospital stay was found to be significantly higher in deceased patients (p = 0.02; Table I). When the gender distribution of the surviving and deceased patients was examined, the mortality rate was found to be 4.889 times higher in men than in women, and a significant difference was observed (p = 0.01; Table II). When the mean operation time and fracture types of the surviving and deceased patients were checked, no significant difference was seen between the two groups (Table I, Table II). The mean operation time of the surviving group was 94.61 ± 31.03 min, and the corresponding value was 95.47 ± 30.56 min in the deceased group (Table I).

Discussion

Hip fracture is one of the leading issues associated with serious mortality and morbidity rates in elderly patients. In our study, we found that a preoperative NPR value of over 38.286 was associated with postoperative one-year mortality in elderly hip fracture patients. In addition, length of hospital stay and the male gender were also associated with one-year mortality.

Neutrophils are known as the group of cells that create the first response to inflammation (14). Stress-induced hormonal changes, such as cortisol secretion, increase neutrophil counts through vascular demargination in hip fracture patients (15). Platelets play an important role in inflammation and its resolution process, despite the fact that they are known to be mainly involved in hemostasis and immunothrombosis. There is also the view that hemostasis and inflammation are closely correlated pathophysiological processes (14). The NPR has been suggested as a systemic inflammation marker that can be calculated with a complete blood count; it is also low cost, easily accessible, and can quickly provide results (10). However, there are no publications in the literature on the correlation between the NPR and postoperative prognosis and mortality of patients with hip fractures.

Muscle injury caused by hip fractures may produce an excessive inflammatory response (8). Recently, more attention has been paid to the correlation between inflammation and prognosis, particularly in elderly individuals (1). In rat models, the correlation between high systemic inflammation observed after hip fracture and acute lung injury has been demonstrated, and lung injury has been found to be more severe in the elderly than in the young (16). It has also been shown that the IL-6 level is correlated with one-year mortality in hip fractures over 80 years of age, and systemic inflammation-associated markers, such as CRP, suPAR, and ferritin, are linked with 30-day mortality after hip fracture (1). Capkın et al. suggested that a CRP/albumin ratio above 2.49 was correlated with postoperative one-year mortality in elderly patients who underwent hemiarthroplasty due to hip fractures (4). In the study by Sökmen et al., in patients over 65 years of age who had undergone hemiarthroplasty for hip fracture, a CRP/albumin ratio of ≥ 29 , being over 85 years old, and having three or more comorbidities were associated with mortality (17). Temiz et al. also checked the correlation between postoperative survival and the NLR at the time of admission to the hospital in patients over 65 years of age who had hip fractures and underwent hemiarthroplasty, and it was shown that a high NLR value was correlated with mortality.

The NLR value has been defined as a marker of systemic inflammation (2). Wang et al. investigated the correlation between the SII, a value calculated over peripheral neutrophils, platelets, and lymphocytes, and postoperative one-year and total mortality; in this case, they found a correlation between the SII and mortality (1). Like these parameters, the NPR is also considered a marker of systemic inflammation. There are publications on various inflammation-associated diseases showing that the NPR can be used as a prognostic factor and a mortality marker. For instance, an increased NPR was found to be correlated with long-term mortality outcomes during hospital stays in infective endocarditis patients (13,18). Likewise, the NPR exhibited superior diagnostic performance in ulcerative colitis patients with clinical and endoscopic

activity compared to other serum biomarkers (CRP, albumin, and ESR) and could identify these patients without the need for expensive biomarkers or colonoscopy (10). Our study revealed that the NPR could also be used in such a way, like the inflammation biomarkers used in previous publications on the elderly population with hip fractures, and determined a correlation between the NPR and the one-year mortality of the geriatric patient population undergoing hip fracture surgery. With the ROC curve analysis, the cut-off value for the preoperative NPR was specified as 38.286, which was found to be significantly higher in patients who died in the postoperative one-year period.

In the systematic literature review by Yu Xu et al. on hip fractures, it was found that the male gender was correlated with poor prognosis and mortality in most studies. Moreover, it has been asserted that there are many predictive factors associated with poor functional outcomes and mortality (19). In a study conducted by Bicen et al. on patients undergoing hip fracture surgery, it was reported that age, male gender, preoperative hemoglobin level, and comorbidities affected mortality (20). Likewise, in our study, postoperative one-year mortality was higher in male patients, and mortality was found to be 4.889 times higher in men than in women.

Yoo et al. investigated the relationship between the length of hospital stay and one-year mortality after hip fracture operations and reported that 604 (14.3%) of 4,213 patients died within one year, and the mortality rate (21.7%) was the highest in patients hospitalized for 10 days or less (21). In a cohort study conducted in the United States, however, a low number of hospital stay days was correlated with reduced postoperative 30-day mortality (22). In our study, the length of hospital stay was observed to be significantly longer in the deceased group. Some studies have identified a relationship between advanced age, extracapsular fractures, and mortality. Despite the presence of studies that have found a link between a high ASA score and mortality, there are also publications indicating that the ASA score is not a determinant of mortality (19). In our study, no correlation was revealed between age, duration of surgery, ASA score, number of comorbidities, fracture type, and postoperative one-year mortality. These differences between the studies most likely result from the fact that mortality is impacted by multifactorial causes.

The limitations of our study consist of the non-inclusion of some variables that might affect survival, such as the level of albumin, the time between the occurrence of the fracture and hospital admission, and body mass index. Our patients' complete blood count values only at the time of admission to the hospital were used, and NPR values in other postoperative periods could be included in further studies. Since our study was carried out retrospectively with medical records and telephone calls, the reasons why the patients had deceased were not exactly known. Therefore, this factor was not included in the study.

Conclusion

In conclusion, our study found that a preoperative NPR value above 38,286 can be an indicator for predicting the mortality of patients over 65 undergoing hip fracture surgery in the postoperative one-year period. Male gender and length of hospital stay were also correlated with postoperative 1-year

mortality. Based on our data, NPR can be used as a simple and economical biomarker in predicting prognosis in geriatric hip fracture patients.

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